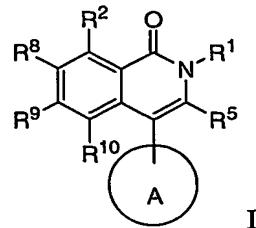


WHAT IS CLAIMED IS:

1. A compound of the structure:



5 or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

- a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with
 - 1) halogen,
 - 2) NO₂,
 - 3) CN,
 - 4) CR⁴⁶=C(R⁴⁷R⁴⁸)₂,
 - 5) C≡C R⁴⁶,
 - 6) (CRⁱR^j)_rOR⁴⁶,
 - 7) (CRⁱR^j)_rN(R⁴⁶R⁴⁷),
 - 8) (CRⁱR^j)_rC(O)R⁴⁶,
 - 9) (CRⁱR^j)_rC(O)OR⁴⁶,
 - 10) (CRⁱR^j)_rR⁴⁶,
 - 11) (CRⁱR^j)_rS(O)0-2R⁶¹,
 - 12) (CRⁱR^j)_rS(O)0-2N(R⁴⁶R⁴⁷),
 - 13) OS(O)0-2R⁶¹,
 - 14) N(R⁴⁶)C(O)R⁴⁷,
 - 15) N(R⁴⁶)S(O)0-2R⁶¹,
 - 16) (CRⁱR^j)_rN(R⁴⁶)R⁶¹,
 - 17) (CRⁱR^j)_rN(R⁴⁶)R⁶¹OR⁴⁷,
 - 18) (CRⁱR^j)_rN(R⁴⁶)(CR^kR^l)_sC(O)N(R⁴⁷R⁴⁸),
 - 19) N(R⁴⁶)(CRⁱR^j)_rR⁶¹,
 - 20) N(R⁴⁶)(CRⁱR^j)_rN(R⁴⁷R⁴⁸),
 - 21) (CRⁱR^j)_rC(O)N(R⁴⁷R⁴⁸), or
 - 22) oxo, or

b) a heteroaryl ring selected from the group consisting of

a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S,

a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O and S, and

5 a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S;

10 wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO_2 ,

3) CN ,

4) $\text{CR}^{46}=\text{C}(\text{R}^{47}\text{R}^{48})_2$,

15 5) $\text{C}\equiv\text{CR}^{46}$,

6) $(\text{CR}^i\text{R}^j)_r\text{OR}^{46}$,

7) $(\text{CR}^i\text{R}^j)_r\text{N}(\text{R}^{46}\text{R}^{47})$,

8) $(\text{CR}^i\text{R}^j)_r\text{C}(\text{O})\text{R}^{46}$,

9) $(\text{CR}^i\text{R}^j)_r\text{C}(\text{O})\text{OR}^{46}$,

20 10) $(\text{CR}^i\text{R}^j)_r\text{R}^{46}$,

11) $(\text{CR}^i\text{R}^j)_r\text{S}(\text{O})_0\text{-}2\text{R}^{61}$,

12) $(\text{CR}^i\text{R}^j)_r\text{S}(\text{O})_0\text{-}2\text{N}(\text{R}^{46}\text{R}^{47})$,

13) $\text{OS}(\text{O})_0\text{-}2\text{R}^{61}$,

14) $\text{N}(\text{R}^{46})\text{C}(\text{O})\text{R}^{47}$,

25 15) $\text{N}(\text{R}^{46})\text{S}(\text{O})_0\text{-}2\text{R}^{61}$,

16) $(\text{CR}^i\text{R}^j)_r\text{N}(\text{R}^{46})\text{R}^{61}$,

17) $(\text{CR}^i\text{R}^j)_r\text{N}(\text{R}^{46})\text{R}^{61}\text{OR}^{47}$,

18) $(\text{CR}^i\text{R}^j)_r\text{N}(\text{R}^{46})(\text{CR}^k\text{R}^l)_s\text{C}(\text{O})\text{N}(\text{R}^{47}\text{R}^{48})$,

19) $\text{N}(\text{R}^{46})(\text{CR}^i\text{R}^j)_r\text{R}^{61}$,

30 20) $\text{N}(\text{R}^{46})(\text{CR}^i\text{R}^j)_r\text{N}(\text{R}^{47}\text{R}^{48})$,

21) $(\text{CR}^i\text{R}^j)_r\text{C}(\text{O})\text{N}(\text{R}^{47}\text{R}^{48})$, or

22) oxo;

R¹ is selected from the group consisting of

35 1) hydrogen,

2) $(\text{CR}^a\text{R}^b)_n\text{R}^{40}$

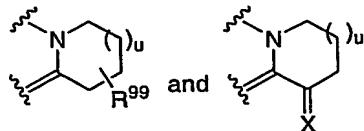
3) $(CR^aR^b)_nOR^{40}$,
 4) $(CR^aR^b)_nN(R^{40}R^{41})$,
 5) $(CR^aR^b)_nN(R^{40})C(O)OR^{41}$,
 6) $(CR^aR^b)_nN(R^{40})(CR^cR^d)_2N(R^{41})C(O)R^{49}$,
 5
 7) C_{3-8} cycloalkyl,
 8) $(CR^aR^b)_nC(O)OR^{40}$,
 9) $(CR^aR^b)_nN(R^{40})(CR^cR^d)_{1-3}R^{41}$,
 10) $(CR^aR^b)_nS(O)_{0-2}R^6$,
 11) $(CR^aR^b)_nS(O)_{0-2}N(R^{40}R^{41})$,
 10
 12) $(CR^aR^b)_nN(R^{40})R^6OR^{41}$,
 13) $(CR^aR^b)_nN(R^{40})(CR^cR^d)_{0-6}C(O)N(R^{41}R^{42})$;

R^5 is selected from the group consisting of

15
 1) hydrogen,
 2) halogen,
 3) $S(O)_{0-2}N(R^{53}R^{50})$,
 4) $S(O)_{0-2}R^{62}$,
 5) CH_3 ,
 6) C_3-C_6 alkyl,
 7) C_3-C_{10} cycloalkyl,
 20
 8) R^{82} ,

25
 said alkyl, and cycloalkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ;

or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



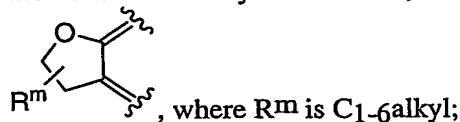
where u is 0 or 1, R^{99} is hydrogen or $-OH$, and X is O or ---NOH ;

R^2 , R^8 , R^9 and R^{10} are independently selected from:

30
 1) hydrogen,

2) halogen,
 3) NO_2 ,
 4) CN ,
 5) $\text{CR}^{43}=\text{C}(\text{R}^{44}\text{R}^{45})$,
 6) $\text{C}\equiv\text{CR}^{43}$,
 7) $(\text{CReRF})_p\text{OR}^{43}$,
 8) $(\text{CReRF})_p\text{N}(\text{R}^{43}\text{R}^{44})$,
 9) $(\text{CReRF})_p\text{C}(\text{O})\text{R}^{43}$,
 10) $(\text{CReRF})_p\text{C}(\text{O})\text{OR}^{43}$,
 11) $(\text{CReRF})_p\text{R}^{43}$,
 12) $(\text{CReRF})_p\text{S}(\text{O})_0\text{-}2\text{R}^{60}$,
 13) $(\text{CReRF})_p\text{S}(\text{O})_0\text{-}2\text{N}(\text{R}^{43}\text{R}^{44})$,
 14) $\text{OS}(\text{O})_0\text{-}2\text{R}^{60}$,
 15) $\text{N}(\text{R}^{43})\text{C}(\text{O})\text{R}^{44}$,
 16) $\text{N}(\text{R}^{43})\text{S}(\text{O})_0\text{-}2\text{R}^{60}$,
 17) $(\text{CReRF})_p\text{N}(\text{R}^{43})\text{R}^{60}$,
 18) $(\text{CReRF})_p\text{N}(\text{R}^{43})\text{R}^{60}\text{OR}^{44}$,
 19) $(\text{CReRF})_p\text{N}(\text{R}^{43})(\text{CR}^8\text{R}^h)_q\text{C}(\text{O})\text{N}(\text{R}^{44}\text{R}^{45})$,
 20) $\text{N}(\text{R}^{43})(\text{CReRF})_p\text{R}^{60}$,
 21) $\text{N}(\text{R}^{43})(\text{CReRF})_p\text{N}(\text{R}^{44}\text{R}^{45})$, and
 22) $(\text{CReRF})_p\text{C}(\text{O})\text{N}(\text{R}^{43}\text{R}^{44})$,

or R^2 and R^8 are independently as defined above, and R^9 and R^{10} , together with the atoms to which they are attached, form the ring



25 $R_a, R_b, R_c, R_d, R_e, R_f, R_g, R_h, R_i, R_j, R_k$, and R_l are independently selected from the group consisting of:

- 1) hydrogen,
- 2) C_1-C_6 alkyl,
- 3) halogen,
- 4) aryl,
- 5) R^{80} ,
- 6) C_3-C_{10} cycloalkyl, and
- 7) OR^4 ,

30

5 said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R⁷, disubstituted with R⁷ and R¹⁵, trisubstituted with R⁷, R¹⁵ and R¹⁶, or tetrasubstituted with R⁷, R¹⁵, R¹⁶ and R¹⁷;

10 R⁴, R⁴⁰, R⁴¹, R⁴², R⁴³, R⁴⁴, R⁴⁵, R⁴⁶, R⁴⁷, R⁴⁸, R⁴⁹, R⁵⁰, R⁵¹, R⁵², and R⁵³ and are independently selected from the group consisting of

- 1) hydrogen,
- 2) C₁-C₆ alkyl,
- 3) C₃-C₁₀ cycloalkyl,
- 4) aryl,
- 5) R⁸¹,
- 6) CF₃,
- 7) C₂-C₆ alkenyl, and
- 8) C₂-C₆ alkynyl,

15 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R¹⁸, di-substituted with R¹⁸ and R¹⁹, tri-substituted with R¹⁸, R¹⁹ and R²⁰, or tetra-substituted with R¹⁸, R¹⁹, R²⁰ and R²¹;

20 R₆, R₆₀, R₆₁, R₆₂ and R₆₃ are independently selected from the group consisting of

- 1) C₁-C₆ alkyl,
- 2) aryl,
- 3) R⁸³, and
- 4) C₃-C₁₀ cycloalkyl;

25 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R²⁶, di-substituted with R²⁶ and R²⁷, tri-substituted with R²⁶, R²⁷ and R²⁸, or tetra-substituted with R²⁶, R²⁷, R²⁸ and R²⁹;

28 R⁷, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵, R²⁶, R²⁷, R²⁸, and R²⁹ are independently selected from the group consisting of

- 1) C₁-C₆ alkyl,
- 2) halogen,
- 3) OR⁵¹,
- 4) CF₃,
- 5) aryl,

- 6) C₃-C₁₀ cycloalkyl,
- 7) R⁸⁴,
- 8) S(O)₀₋₂N(R⁵¹R⁵²),
- 9) C(O)OR⁵¹,
- 5 10) C(O)R⁵¹,
- 11) CN,
- 12) C(O)N(R⁵¹R⁵²),
- 13) N(R⁵¹)C(O)R⁵²,
- 14) S(O)₀₋₂R⁶³,
- 10 15) NO₂, and
- 16) N(R⁵¹R⁵²);

R⁸⁰, R⁸¹, R⁸², R⁸³ and R⁸⁴ are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting of N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6;
provided that

when R⁹ is OCH₃, R¹ is CH₃ and R⁵ is C(CH₃)₃, then A is substituted,

20 when R⁹ is hydrogen, R¹ is CH₃, and R⁵ is hydrogen, then A is substituted,

when R⁹ is hydrogen, R¹ is CH₃, and R⁵ is C(CH₃)₃, then A is substituted, provided the substituent is not CH₃, and

when R⁹ is OCH₃, R¹ is CH₃, R⁵ is CH₃, then A is substituted.

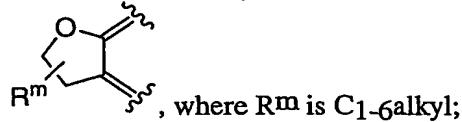
2. A compound of Claim 1, or a pharmaceutically acceptable salt thereof, wherein
25 A is an aryl ring selected from phenyl, unsubstituted or substituted as in Claim 1, or a heteroaryl ring, unsubstituted or substituted as in Claim 1, selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, indole, pyrrolopyridine, benzimidazole, benzoxazole, benzothiazole, and benzoxadiazole;

R², R⁸, R⁹ and R¹⁰ are independently selected from the group consisting of:

- 30 1) hydrogen,
- 2) halogen,
- 3) OR⁴³,
- 4) (C_{Re}R_f)_pR⁴³,
- 5) CN, and

6) $(CReRf)_pC(O)N(R^43R^44)$,

or R^2 and R^8 are independently as defined above, and R^9 and R^{10} , together with the atoms to which they are attached, form the ring



5 R^1 is selected from the group consisting of

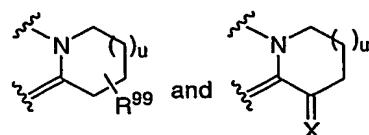
- 1) hydrogen,
- 2) $(CReRf)_{1-2}R^40$
- 3) $(CReRf)_{1-2}OR^40$,
- 4) $(CReRf)_{1-2}N(R^40R^41)$,
- 5) $(CReRf)_{1-2}N(R^40)C(O)OR^41$,
- 6) $(CReRf)_{1-2}N(R^40)(CRCRd)_{2-3}N(R^41)C(O)R^49$,
- 7) $(CReRf)_{1-2}C(O)OR^40$,
- 8) $(CReRf)_{1-2}N(R^40)(CRCRd)_{1-3}R^41$, and
- 9) cyclopropyl; and

15 R^5 is selected from the group consisting of

- 1) hydrogen,
- 2) halogen,
- 3) $S(O)_{0-2}N(R^53R^50)$,
- 4) $S(O)_{0-2}R^62$,
- 5) CH_3 ,
- 6) C_3-C_6 alkyl,
- 7) C_3-C_{10} cycloalkyl,
- 8) R^82 ,

25 said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ,

30 or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



where u is 0 or 1, R^{99} is hydrogen or $-OH$, and X is O or $\ddot{N}NOH$.

3. A compound of Claim 2, or a pharmaceutically acceptable salt thereof, wherein R^2 , R^8 , R^9 and R^{10} are independently selected from the group consisting of:

5

- 1) hydrogen,
- 2) halogen,
- 3) OR^{43} , and
- 4) $(CRERF)_pC(O)N(R^{43}R^{44})$.

4. A compound of Claim 3, or a pharmaceutically acceptable salt thereof, wherein 10 R^1 is selected from the group consisting of

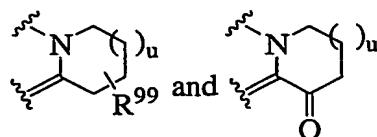
- 1) hydrogen,
- 2) $(CRArb)_{1-2}R^{40}$
- 3) $(CRArb)_{1-2}OR^{40}$, or
- 4) $(CRArb)_{1-2}N(R^{40}R^{41})$;

15 R^5 is selected from the group consisting of

- 1) hydrogen,
- 2) C_3-C_6 alkyl, and
- 3) CH_3 ,

20 said alkyl is unsubstituted, mono-substituted with R^{22} , di-substituted with R^{22} and R^{23} , tri-substituted with R^{22} , R^{23} and R^{24} , or tetra-substituted with R^{22} , R^{23} , R^{24} and R^{25} ;

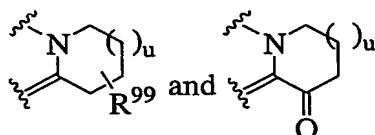
or R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



25 where u is 1, and R^{99} is hydrogen or $-OH$.

5. A compound of Claim 4, or a pharmaceutically acceptable salt thereof, wherein A is unsubstituted phenyl, or phenyl substituted with halogen.

6. A compound of Claim 5, or a pharmaceutically acceptable salt thereof, wherein 5 R¹ is selected from the group consisting of -CH₃, -CH₂CH₃, -(CH₂)₂OCH₃, -(CH₂)₂NH₂, and -(CH₂)₃NH₂, -CH₂C(O)OC(CH₃)₃; and R⁵ is selected from the group consisting of hydrogen, -C(CH₃)₃, -CH₃, or R¹ and R⁵ together with the atoms to which they are attached, form a ring selected from the group of 10 structures consisting of



where u is 1, and R⁹⁹ is hydrogen or -OH.

7. A compound of Claim 6, or a pharmaceutically acceptable salt thereof, selected from the group consisting of

15 3-tert-butyl-4-(3-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,
 3-tert-butyl-4-(4-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,
 20 6-methoxy-2-methyl-4-phenylisoquinolin-1(2H)-one,
 4-(3-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,
 4-(4-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,
 25 (1E)-11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione 1-oxime,
 3-tert-butyl-6-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

2,3-dimethyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-ethyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

5 3-tert-butyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

2-ethyl-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

10 6-methoxy-2-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1(2H)-one,

2-(2-aminoethyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

15 2-(3-aminopropyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carbonitrile,

3-tert-butyl-8-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

20 3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carboxamide,

3-tert-butyl-2-methyl-4-phenyl-6-(4-phenylbutoxy)isoquinolin-1(2H)-one,

25 3-tert-butyl-2-methyl-4-phenyl-6-[(5-phenylpentyl)oxy]isoquinolin-1(2H)-one,

11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione,

(+/-)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

30 (1*S*)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

(1*R*)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one, and

11-(3-fluorophenyl)-9-methoxy-1,2,3,4-tetrahydro-6*H*-pyrido[1,2-*b*]isoquinolin-6-one.

5

8. A method of treating a condition in a mammal, the treatment of which is effected or facilitated by $K_{v1.5}$ inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting $K_{v1.5}$.

10

9. A method of Claim 8, wherein the condition is cardiac arrhythmia.

10. A method of Claim 9, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

15

11. A method of Claim 10, wherein the cardiac arrhythmia is atrial fibrillation.

12. A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by $K_{v1.5}$ inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting $K_{v1.5}$.

20

13. A method of Claim 12, wherein the condition is cardiac arrhythmia.

14. A method of Claim 13, wherein the cardiac arrhythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

25

15. A method of Claim 14, wherein the cardiac arrhythmia is atrial fibrillation.

16. A method of Claim 12, wherein the condition is a thromboembolic event.

30

17. A method of Claim 16, wherein the thromboembolic event is a stroke.

18. A method of Claim 12, wherein the condition is congestive heart failure.

19. A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim 1 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

5 21. A method of treating cardiac arrhythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa 10 inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

15 22. A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.